Incorporating Vestibular Evoked Myogenic Potential (VEMP) Assessment into Our Clinical Practice

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Vestibular Evoked Myogenic Potentials (VEMPs) are short-latency electromyographic responses evoked by intense acoustic stimuli. They are measured in the ipsilateral, tonically-contracted sternocleidomastoid (SCM) muscle. The VEMP response is thought to arise from the vestibulocollic (also called sacculocollic) reflex. Since its introduction in 1992 (Colebatch et al.), VEMP testing is gradually becoming a part of standard vestibular assessment in many clinics. VEMPs have been found in response to various stimuli including loud clicks, short tone bursts, head taps and short duration DC currents presented to the mastoid. (Colebatch et al., 1994; Murofushi et al., 1996; Akin & Murnane, 2001; Cheng & Murofushi, 2001; Colebatch, 2001; de Waele, 2001; Ödkvist, 2001; Basta et al., 2005). The purpose of this article is to review the literature on VEMP testing in an effort to determine the clinical, best practice of their use. We will explore the recommended measurement parameters, what constitutes a normal response, how several types of pathology affect VEMPs and why we should consider incorporating VEMP assessment into our standard vestibular evaluation protocol.

Origin of the VEMP Response

The saccule is the vestibular organ that is most sensitive to acoustic stimuli. This is possibly because it lies in close proximity to the stapes footplate where it can receive impact from sound acting on the tympanic membrane (Halmagyi & Curthoys, 1999). Mc Cue & Guinan, Jr. (1997) found that the saccule is innervated by acoustically responsive

afferent fibers with an irregular discharge, which respond to sound with a latency that is shorter than that observed with cochlear fibers. These saccular afferents exhibit higher thresholds for acoustic stimuli than do cochlear afferents and have been found to be specifically responsive only in the frequency range of 100 to 3000 Hz. It is thought that this response to loud acoustic stimulation arises from endolymph movement in the sound-sensitive saccule, which, in turn, results in the presence of an inhibitory response (decrease in motor neuron firing rate) in the cervical flexor motor neurons via the vestibulo-spinal tract (Murofushi et al., 1996; Halmagyi & Curthoys, 1999; de Waele, 2001; Ödkvist, 2001; Clarke et al., 2003).

Colebatch and his colleagues (1992, 1994) identified a biphasic response in SCM muscle activity to loud acoustic stimuli, namely the positive p13 wave and the negative n23 wave, predominately arising from the side ipsilateral to the ear being stimulated (see also Akin & Murnane, 2001). They further identified less common, later responses, the n34 and p44 potentials, which were found to occur bilaterally in response to unilateral ear stimulation. Waves p13 and n23 are believed to arise from saccular afferent activity that is transmitted via the oligosynaptic pathways (includes activation of the saccule, vestibular afferent conduction via the inferior vestibular nerve to the vestibular nucleus, central conduction to the motor nucleus of the SCM through the vestibulospinal tract) to the anterior neck muscles. The later potentials, n34 and p44, are thought to be of cochlear origin since they are not dependent upon the integrity of the vestibular nerve (Colebatch et al., 1994; de Waele, 2001; Ozeki et. al., 2005; Akkuzu et al., 2006). Basta and colleagues (2005[2]) measured VEMP responses intraoperatively via direct stimulation

of the inferior vestibular nerve. They found that the VEMP response is in no way mediated by the superior vestibular nerve or the cochlear nerve.

VEMP Measurement

VEMPs are typically measured using loud clicks (90-110 dB nHL) presented monaurally or binaurally via calibrated headphones or insert phones at a rate of 3-6 Hz To obtain the VEMP, EMG activity in response to the intense stimuli as measured from the SCM muscle is amplified, bandpass filtered and averaged. At least two trials of 100 runs should be obtained for each ear to ensure that the response is repeatable (Colebatch et al., 1994; Murofushi et al., 1996; Heide et al., 1999; Murofushi et al., 1999; Brantberg & Fransson, 2001; Colebatch, 2001; de Waele, 2001; Ödkvist, 2001; Young et al., 2002[2]; Clarke et al., 2003). Several factors have been found to influence the VEMP recording. For example, Huang and colleagues (2005) recommended the use of a 0.5 ms click duration to evoke VEMPs because it resulted in better waveform morphology, smaller interaural differences in normal subjects and was found to be produced in normal subjects more often (100% of the time) than with clicks with a duration of 0.1 ms (94% of the time). Additionally, it has been found that the higher the intensity of the acoustic stimuli, the larger the amplitude of the VEMP; and the higher the rate of stimulation, the smaller the VEMP amplitude (Wu & Murofushi, 1999; Akin & Murnane, 2001; Brantberg & Fransson, 2001; Ochi et al., 2001). With regards to the stimulation rate, Sheykholesami and colleagues (2001[2]) suggested that the rate of acoustic stimuli presentation should be slow enough to prevent adaptation of the response, but fast enough to be clinically applicable. Wu & Murofushi (1999) found that wave amplitude was greatest for

stimulation rates of 1 and 5 Hz. They also found that variance was greatest for responses to faster stimulation rates (20 Hz) than it was to slower stimulation rates (1 Hz). They, therefore, recommended the use of a 5 Hz stimulation rate as a compromise between patient comfort (shorter test time than 1 Hz) and reliability (much greater than for 20 Hz) for clinical use of VEMPs.

Murofushi and colleagues (1999) found that short tone bursts were also able to evoke VEMPs in normal subjects, with tone bursts of 500 Hz evoking the largest response of any frequency of stimulation (when compared to 1 and 2 kHz; and as later investigated by Node et al., 2005, when compared to 0.25, 0.75, 1, 1.5, 2 and 4 kHz). They further found that, in some instances, stimulation via short tone bursts had resulted in normal results when the click-evoked VEMP had been abnormal, and vice versa. Therefore, they recommended the use of both click and short tone burst stimuli to confirm VEMP responses (Murofushi et al., 1999, n = 9 normal subjects and 30 patients with vestibular disorders). Cheng, Huang & Young (2003; n = 29 normal subjects) found that click-evoked VEMPs were present in more normal ears (98%) than tone burst-evoked VEMPs were (88%). The VEMPs evoked by loud clicks exhibited a shorter latency and larger amplitude than short tone burst-evoked VEMPs. Based on these findings, the authors suggested that the use of a click stimulus should be preferred over short tone bursts. In the largest study evaluating this relationship between clicks and tone bursts, Patko and colleagues (2003; n = 95 normal subjects and 170 subjects with unilateral acoustic neuroma) found that short tone burst evoked VEMPs were always normal in patients who had normal VEMPs in response to click-evoked VEMPs. However, when click-evoked VEMPs were abnormal in these subjects, short tone burst-

evoked VEMPs were either normal or had low amplitude. Therefore, the authors suggested that click-evoked VEMPs and short tone burst-evoked VEMPs provided complimentary information about saccular function; while clicks may provide evidence of minor saccular dysfunction, short tone bursts may provide information about the presence of any residual function of the saccular nerve (Patko et al., 2003).

In addition to the frequency of the tone burst, the plateau time of the stimulus can also affect the VEMP response that is observed. The larger the plateau time, the greater the p13 and n23 latencies and the greater the interval between them. In one study, the smallest amount of variance was found for the 2 ms plateau time, thereby causing the smallest normal interaural differences. The VEMP amplitude was lowest with the 1 ms plateau time, but was comparable to the other plateau times (Cheng & Murofushi, 2001). Therefore, Cheng & Murofushi (2001) recommended the use of a 500 Hz tone burst at a repetition rate of 5 Hz, a 1 ms rise and fall time, and 2ms plateau time. This type of stimuli resulted in the most consistent VEMP response and the best overall waveform morphology.

Binaural acoustic stimulation can be presented when recording VEMPs as a more time efficient and comfortable means of acquiring such data, as it requires less data collection time and, therefore, overall less muscular effort (Wang & Young, 2003). Bhagat (2006) compared monaural and binaural acoustic stimuli of varying frequencies (250, 500, 750 and 1000 Hz) for unilateral contraction of the SCM muscle (with patients in a supine position with their head lifted and turned toward the side of testing) to assess the affect of monaural/binaural stimulation on the unilateral VEMP response. This study found that relative magnitude was lowest for binaural acoustic stimulation (7-17% lower

than with monaural stimulation). The authors hypothesized that crossover myogenic activity could interfere with unilateral measurement of VEMPs with high-level binaural stimuli, possibly due to the stapedial reflex (which may be more responsive with binaural stimulation). However, no difference was observed in the p13 or n23 wave latencies with binaural versus monaural stimulation. Huang et al. (2006) found latencies of p13 and n23 to be significantly shorter when using a binaural stimulation, compared to a monaural. They found no significant amplitude difference between monaural and binaural stimulations. In this study, subjects also used a bilateral contraction of the SCM muscles by lying in the supine position with head elevated. Wang & Young (2003) found that VEMP responses were similar with monaural and binaural acoustic stimulation. They concluded that binaural acoustic stimulation could be used to obtain equivalent response rate, latencies, and interaural difference in subjects with normal vestibular function and in patients with vestibular disease. Since the response to binaural acoustic stimulation is similar to the response to monaural stimulation, acoustic stimuli can be presented binaurally to screen for asymmetry in order to reduce testing time. If asymmetry is noted during such a screening, VEMPs obtained by unilateral, monaural stimulation should be obtained (Brantberg & Fransson, 2001). The confounding evidence further highlights the need to establish norms that are specific to the equipment and protocol that will be used.

VEMP activity is typically measured via a surface electrode on the belly of the SCM muscle, with the reference electrode placement at the site of the sternoclavicular junction or upper sternum, and the ground electrode placed on the forehead (Colebatch et al., 1994; Heide et al., 1999; de Waele, 2001; Clarke et al., 2003). Other electrode montages have been used as well, depending on the function of the recording equipment

(for example, recording electrode on belly of SCM, reference electrode on sternoclavicular junction and ground electrode on the contralateral SCM for systems that perform automatic switching – Wang et al., 2006; Picciotti et al., 2007). Short latency responses are measured at the electrode that is located on the SCM. These responses are quite large (60-300 mV) (Akin & Murnane, 2001; Ödkvist, 2001). In order to obtain an optimal recording, electrode impedance should be held below 3-5 kΩ (Basta et al., 2005[1]).

Some authors have presented VEMP stimuli with a continuous noise (Heide et al., 1999; Takegoshi & Murofushi, 2003). White noise presented contralaterally and ipsilaterally to the stimulus ear has been shown to decrease VEMP amplitude, especially with higher intensities of white noise presentation. This supports the hypothesis that cochlear afferents are capable of influencing the amplitude of the VEMP response through the stapedial reflex (Takegoshi & Murofushi, 2003).

Studies have shown that the greater the mean level of rectified, baseline tonic EMG activity, the greater the amplitude of the evoked response. A SCM contraction resulting in an activity level of 50-200μV is optimal for obtaining VEMP responses (Colebatch et al., 1994; Akin & Murnane, 2001). Subjects can activate their SCM muscle in a variety of ways. Initially, SCM contraction was evoked when sitting upright by having subjects push their heads against a padded bar (Colebatch et al., 1994). To activate the SCM muscles symmetrically and bilaterally, the subject may lie in the prone position while lifting the head (Colebatch et al., 1994; de Waele, 2001; Ödkvist, 2001). The subject lying in the supine position may also be asked to simply turn their head away from the ear receiving the acoustic stimulation, thereby contracting the ipsilateral SCM

muscle (Colebatch et al., 1994; Murofushi et al., 1999). Isaacson et al. (2006) assessed VEMP responses when using three different head positions to activate the SCM. Specifically, they had subjects sit with the head turned away from the test ear (while pressing their head against their hand), lie supine with the head held straight up, and lie supine with the head held up and turned away from the test ear. The authors found no significant difference in wave latencies or corrected VEMP amplitudes (amplitude that has been corrected for the baseline level of tonic SCM activation). They concluded that VEMP amplitude had a positive correlation to level of SCM EMG activation. They suggested that positioning the subject's trunk 30 degrees above horizontal prior to having them lift their head may make SCM stimulation from a supine position more comfortable, resulting in less fatigue and overall effort needed.

It has been shown that less variability is seen in VEMP amplitude when SCM muscle activity is monitored to maintain a constant level of activation (Colebatch et al., 1994; Murofushi et al., 1999; Vanspauwen et al., 2006). Some research centers have incorporated the use of EMG monitoring equipment for this reason. However, most currently available EP equipment is unable to monitor both EMG and VEMP responses at the same time. EMG activity may be recorded via a two-channel stand-alone unit. The differential surface electrode is placed on the SCM muscle near the VEMP electrode while the reference electrode is attached to the wrist. The EMG signals are amplified (10,000 times), bandpass filtered from 20 to 450 Hz, and digitized at 1024 Hz. The level of EMG activity is then presented on a computer monitor to provide visual feedback to the subject (Akin & Murnane, 2001). EMG activity can also be displayed on a screen using an oscilloscope or with a light-emitting diode bar. A target level can be identified

on the screen and the subject will be encouraged to maintain a constant level of EMG activity just above the target throughout the recording period. This corresponds to about 30-60 μV of muscular activity (Colebatch et al., 1994; Murofushi et al., 1996; Akin & Murnane, 2001; Murofushi et al., 2001).

Vanspauwen, Wuyts & Van de Heyning (2006) proposed a novel method by which to monitor SCM contraction during VEMP testing, without the purchase of additional expensive EMG equipment. Particularly, this feedback method requires that the patient push their jaw against a hand-held blood pressure cuff in an effort to maintain a specific cuff pressure as read on the manometer. The procedure involves inflation of the blood pressure cuff to a preset level of 20 mm Hg. The patient then flexes their head 30 degrees forward and rotates it 30 degrees to the side opposite testing. While holding the cuff between the patient's hand and jaw, the patient pushes their jaw into the cuff to generate a pressure of 40 mm Hg. When using this type of feedback method, variability in amplitude differences was greatly reduced (from 104 μV, SD = 72 μV without feedback to 34 μV, SD 25μV with the cuff feedback system). Certainly, using some form of SCM contraction feedback will result in more reliability of left-right VEMP amplitude differences.

Several parameters of the VEMP response may be assessed to determine the presence of pathology. VEMP threshold is determined by finding the lowest stimulus level that can produce repeatable characteristic VEMP waveforms at the appropriate latencies. Although threshold has been found to be quite variable in some cases, it has also been found to be the most sensitive way to identify disorders such as Superior Canal Dehiscence when it is especially low (Isaacson et al., 2006). VEMP latencies may also

be assessed to provide information about disorders that may affect neural conduction, such as Multiple sclerosis. VEMP wave amplitudes are measured either from a single peak in reference to the mean level of EMG activity before the acoustic stimuli is presented or from peak-to-peak (Colebatch et al., 1994). However, VEMP measurement may prove most useful when comparing the response from one side to the response from the other side, including differences in threshold, amplitude and latency. It must be remembered, however, that minor differences in latency and amplitude can occur merely from minor differences in electrode placement or differences in muscle anatomy. Therefore, it has been suggested that asymmetries of 2.5:1 can be taken as evidence of pathological vestibular asymmetry (Halmagyi & Curthoys, 1999; Ochi et al., 2001).

Some authors have used an evoked potential (EP) ratio (also called a VEMP Asymmetry – VA - ratio), that is

$$100[(A_{left}-A_{rightl})/(A_{left}+A_{right})]$$

where A_{left} indicates the amplitude on the left side and A_{right} indicates the amplitude on the right side to compare responses on one side to responses on the other side. This formula has been used to compare interaural difference in the VEMP amplitude. However, no significant difference has been found between EP ratios for normals and EP ratios for subjects with peripheral vestibular disorders, especially when using values above the mean plus two standard deviations (~59.7% difference) as your criterion for abnormal values (Heide et al., 1999; Murofushi et al., 1999; Akkuzu et al., 2006). Basta and colleagues (2005[1]) suggested that because inter- and intra-individual differences are vast, comparison between ears using monaural testing may not be appropriate. However, subjects in their study did not have a means of feedback to monitor SCM activation.

Perhaps if a method of EMG activity monitoring or a bilateral contraction of the SCM muscles were used, a significant difference would emerge. Further research needs to look specifically at the value of comparing between ears when using feedback and/or bilateral SCM stimulation.

For VEMP assessment in subjects with conductive hearing loss, bone conducted (BC) clicks and tone bursts (both presented at 70 dB HL – the maximum linear output of the bone oscillator) delivered to the mastoid process were found to elicit a VEMP waveform similar to that obtained with air conducted (AC) stimuli in subjects without conductive hearing loss and normal vestibular function (Sheykholeslami et al., 2001[1]; Bhagat, 2006). One author suggested that BC stimulation of the saccule has little influence from the middle ear system. Therefore, the stapedial reflex would have no bearing on the responses for BC-VEMPs, as has been postulated may play a role in AC-VEMPs with binaural stimulation or with the use of a masking noise (Bhagat, 2006). Sheykholeslami and colleagues (2001[1]) found BC VEMPs obtained via short duration tone bursts to result in higher VEMP amplitude and better waveform morphology than with click stimuli (n = 11, aged 4-20 years); present in all subjects with TB stimuli, absent in 3 subjects with click stimulation). They (2001[2]) also suggested the use of a 10 Hz repetition rate with BC VEMPs because it provides a higher amplitude wave and better waveform, while reducing discomfort of testing by decreasing testing time. They further found that BC VEMPs were most sensitive to stimulus frequencies of 200 and 400 Hz. Another study (n = 18 young adults) obtained tone burst- evoked BC VEMPs in 14 of 18 normal subjects. The authors noted that with BC stimuli, wave p13 consistently occurs at an early latency when compared to AC stimuli, especially when presented

monaurally. Wave n23 also occurs at an earlier latency in the BC condition (Bhagat, 2006). However, no significant latency differences were observed in one study (n = 64 adults; tone burst stimuli) by Basta and colleagues (2005[1]) when comparing responses to AC and BC stimuli. Due to confounding data, in clinical practice normative data should be obtained for AC and BC stimulation separately.

Todd and his colleagues (2007) exploited the finding that acoustic stimulation of the vestibular system evokes potentials in surface electrodes placed close to the eyes. The investigators utilized a 500 Hz tone pip at a rate of 5 Hz for both air- and bone-conducted stimulation. Scleral dual-search coils were used to record horizontal, vertical and torsional eye positions. Subjects laid in the supine position with their gaze directed straight ahead to a target. Extraocular potentials were measured using four electrodes placed in a vertical montage in line with the center of the eye. The authors found extraocular movement that was characterized by a series of positive and negative waves above and below each eye, beginning at about 6ms. The positive going waves occurred, on average, at approximately 8 ms and the initial negative going waves occurred at approximately 10 ms (coined the p8 and n10 responses). A secondary negative going wave was also found to occur around 13 ms (n13). The conclusion was that these extraocular potentials arose from electromyogenic activity of the extraocular muscles, presumed to be analogous to the VEMP response seen with sternocleidomastoid activation. Therefore, these extraocular potentials in response to intense stimuli have been termed *Ocular Vestibular Evoked Myogenic Potentials* (OVEMPS). Based on recording from scleral search coils, small and consistent eye movements were recorded in response to the stimulation that was different between the two types of stimulus

presentation (air-conduction and bone-conduction). Eye movements in response to air-conducted stimuli could be explained by the extraocular eye movements of the OVEMPs. Eye movements related to bone-conducted stimuli results from bilateral stimulation and, therefore, exhibited some variation in horizontal and torsional eye movements. Based on these findings, the authors suggested that the eye movements evoked by air-conducted stimulation were the result of activation of the saccule and that the eye movements evoked by bone-conducted stimulation were the result of activation primarily of the utricle.

In summary of the preceding research findings, the following measurement protocol is recommended. Use of a click stimulus (0.5 ms duration, at a rate of 5 Hz, and an intensity between 90-110 dB nHL) is preferred for initial measurement (Cheng et al., 2003; Patko et al., 2003; Huang et al., 2005). If no response is obtained in response to the click stimuli, the use of a tone burst stimulus (2 ms plateau and 1 ms rise and fall times, 5 Hz rate, and intensity between 90-110 dB nHL) is recommended (Murofushi et al., 1999; Cheng & Murofushi, 2001; Node et al., 2005). The two types of stimuli may provide complimentary information regarding minor saccular dysfunction and residual saccular nerve function (Patko et al., 2003). Also, to reduce test time, a binaural mode of stimulation and SCM muscle contraction may be used. If a quick screening with a binaural stimulus suggests asymmetry, proceed with monaural stimulation for individual ear assessment (Brantberg & Fransson, 2001; Wang & Young, 2005). If the patient is unable to maintain the supine with head elevated position for bilateral SCM contraction, a sitting with head turned contraction will suffice. However, SCM contraction monitoring /feedback is important to reduce inter- and intra-subject variability (Colebatch et al.,

1994; Murofushi et al., 1999; Isaacson et al., 2006; Vanspauwen et al., 2006). VEMP threshold, amplitude, latency and interaural differences in amplitude/latency are important parameters to assess in the VEMP response. In the presence of conductive hearing loss, bone conducted VEMP may be assessed (200 or 400 Hz tone burst with a 10 Hz repetition rate) (Sheykholeslami et al., 2001). It must be realized, however, that there is no universally-established protocol. As research on VEMPs continues to emerge, clinical best practice will become better defined. Research with OVEMPs may eventually lead to a new way to assess the VEMP response that may also allow us to assess utricular function (Todd et al., 2007).

The Normal VEMP Response

VEMP waveforms are observed in almost all normal individuals without conductive hearing loss (Colebatch, 2001). Four waves are typical in the VEMP response: p13, n23, n34, and p44. While waves p13 (mean latency of 12.8-13.3) and n23 (mean latency of 22.6) are thought to arise from ipsilateral connections, waves p34 (mean latency of 33.8) and p44 (mean latency 43.7) arise from bilateral connections (Colebatch et al., 1994; Clarke et al., 2003; Basta et al., 2005[2]). Waves p13 and n23 are present in all subjects with presumed normal vestibular function, even in the presence of bilateral sensorineural hearing loss. Waves n34 and p44, on the other hand, are absent in half of subjects tested with normal hearing and in subjects with bilateral sensorineural hearing loss (Colebatch et al., 1994; de Waele, 2001; Clarke et al., 2003). The p13-n23 complex is only observed with the presentation of intense acoustic stimuli and thresholds for these clicks were found to be between 75 and 95 dB nHL with no significant interaural

differences in normal subjects (Colebatch et al., 1994; Halmagyi & Curthoys, 1999; Ochi et al., 2001). Thresholds for the later potentials, p34 and p44, were found to be consistently lower than this, as low as 50 dB in some patients (Colebatch et al., 1994). The p13/n23 latencies depend heavily on the type of stimulus that is applied (click versus tone burst) and the frequency of stimulation (Basta et al., 2005[1]; see above for a discussion on optimal stimulus selection). The mean peak-to-peak amplitude for p13 and n23 was found to be highly variable among normal subjects and was, therefore, not clinically applicable (de Waele, 2001). However, as previously discussed, comparison between ears of both latency and amplitude may help to separate diseased ears from normal ears. Each clinic should establish their own norms using exactly the same stimulus and collection parameters as will be used in clinical practice.

Some gender differences have been noted in the VEMP response. Brantberg & Fransson (2001) found that women had earlier (0.74 ms sooner on average) occurring p13 waves, but no gender differences were noted in VEMP amplitude or latency of n23, when using clicks. However, Basta and colleagues (2005[1]) found no gender differences for latencies of either the p13 or the n23 waves when using a 500 Hz tone burst stimulus. The differences seen between the two studies may be due to the different stimulus that was used for each study or the tonic muscle contraction. While one study used EMG monitoring to maintain a desired level of activity (Brantberg & Fransson, 2001), the other one used EMG rectifying to control for muscle activity (Basta et al., 2005[1]). Ochi & Ohashi (2003) found a significant correlation between age and VEMP thresholds and the p13-n23 amplitude. Specifically, with increased age, VEMP amplitude decreased. This finding was consistent with the belief that age-related changes occur in the neural and

sensory elements in structures lying along the sacculocollic reflex pathway. Although, the authors point out a possible influence on the VEMPs coming from SCM muscle tension, they state that this contribution is quite small and is not likely to account for the age-related changes in VEMP threshold. When using interaural differences as the primary measurement of interest, age-related changes in the vestibular system can be ignored, because we are looking for absolute differences between the two ears. However, it must be noted that age must be taken into account when evaluating VEMPs for the presence of bilateral lesions (Ochi & Ohashi, 2003; see also Basta et al., 2005[1]). Another study suggested age-related changes in VEMP latency that are thought to be related to physiologic changes in the number of vestibular hair cells, Scarpa's ganglion cells and vestibular cells lying in the brainstem (Basta et al., 2005[1]).

Sheykholesami and colleagues (2005) assessed VEMP responses in infants (ages 1-12 months). SCM activity was maintained by turning the infants head as far as possible to one side and using the routing reflex or audiovisual stimulation. Consistent VEMP responses were recorded that included a p13 and n23 wave, with p13 latency being close to that of adults and n23 latencies reduced compared to adults latencies. Although, more difficult to complete in children (primarily due to attention and maintenance of SCM activity), the authors stated that there is some possible utility in assessing VEMP responses in infants. Specifically, they reported that assessment of otolith organ function in infants can give us information about vestibulocollic function, which may help guide care and rehabilitation in infants at risk for developmental and motor system delay. Erbek and colleagues (2007) found similar results when assessing VEMPs in newborns

and suggested that this test can be reliably carried out on infants at least four weeks of age.

When assessing VEMP responses in children (ages 3-11), Kelsch and his colleagues (2006) found the presence of normal VEMP responses in all children for a 90 dB nHL click. When using 85 and 80 dB nHL clicks, only 50% and 10% of subjects exhibited normal VEMPs, respectively. The authors also showed shorter latencies for both waves p13 and n23, when compared to adults, and especially earlier latencies for the youngest children tested (ages 3-6). They established normative data for children in 3-11 year age range. They also suggested longer P13 latencies for girls than for boys (mean difference of 1.1 seconds). A similar study by Picciotti and her colleagues (2007) found no significant difference in p13 or n23 latencies or amplitude ratio in children when compared to adults or between children in different age groups (3-15 years of age). The differences seen in this study may be related to the difference in stimuli. Picciotti et al. (2007) used a 500 Hz logon stimulus (amplitude modulated pure tone), whereas, Kelsch et al. (2006) used a click stimulus. Assessing VEMPs in children is very feasible. It takes approximately 10-15 minutes to complete testing in both ears. Younger children may require more motivation in order to hold their attention. Some children find the supine with head elevated position to be uncomfortable for long periods of time. Therefore, it has been recommended that the child may be allowed to lie back on their elbows instead of lying supine. This allowed for greater compliance and increased endurance, without significantly affecting the VEMP response (Kelsch et al., 2006; Picciotti et al., 2007). It was concluded that VEMPs may be assessed in children with profound SNHL to evaluate the need for developmental therapy or to guide the decision

of which side to implant for cochlear implant candidates (Kelsch et al., 2006). More research is needed to evaluate the possible role and benefit of VEMPs in assessing vestibular function in newborns and infants (Erbek et al., 2007).

VEMP Responses in Subjects with Hearing Loss

VEMPs are consistently present in subjects with severe sensorineural hearing loss with normal vestibular function. Conductive hearing loss, however, will result in absent VEMPs or VEMPs with decreased amplitude (Colebatch & Halmagyi, 1992; Colebatch et al., 1994; see also Akin & Murnane, 2001 and Ödkvist, 2001). Specifically, one study found VEMPs to be absent, reduced and/or significantly delayed in subjects with Middle Ear Effusion (MEE). Additionally, VEMP asymmetry ratio was significantly increased. Following aspiration of the tympanic membrane, latencies and asymmetry ratio immediately returned to normal values, however, amplitude of the VEMP remained unchanged. The researchers in this study found that the presence of an air-bone gap could not predict the presence or absence of VEMP responses. They went on to suggest that the delayed latencies were likely due to a decrease in energy transfer in the presence of middle ear fluid. The inability of the VEMP amplitude to return to normal values following aspiration may be due in part to the older age of the participants in the study (mean age of 66 years) (Wang & Lee, 2007).

Singbartl et al. (2006) evaluated BC-VEMPs (sitting with head turned toward test ear) in subjects with otosclerosis before and after stapedotomy surgery. Preoperatively, only 44% of otosclerotic ears had regular BC-VEMPs, considering latencies and relative amplitude. In 12% of those with absent VEMPs preoperatively, normal VEMP responses

were seen following stapedotomy surgery. The authors suggested that the absence of BC-VEMPs seen in otosclerotic ears might be due to interaction between the stapes footplate and the saccule, which may be inadequate due to fixation. Yang & Young (2006) compared VEMP responses in patients with otosclerosis using both an AC and BC stimuli (supine with head elevated). They found present AC-VEMPs in 24% of affected ears and BC-VEMPs present in 76% of affected ears. With present VEMPs, no significant difference was found for mean latencies or amplitude when compared to normal ears. It was noted that the mean air-bone gap present in those with absent BC-VEMPs was significantly larger than the mean air-bone gap for those with present responses, with most ears presenting with absent BC-VEMPs having an air-bone gap greater than 30 dB. If BC-VEMPs were absent, so too were AC-VEMPs. However, the opposite could not be said. That is the absence of AC-VEMPs did not negate the presence of BC-VEMPs. The authors suggested that the presence or absence of both AC and BC-VEMPs might provide information about the stage or progression of the otosclerosis. Specifically, they suggested that if AC-VEMPs are present, only localized fixation has occurred and the air-bone gap is less than 30 dB. If BC-VEMPs are absent as well, the disease has progressed to the point were fixation becomes more diffuse or has resulted in anklyosis (stiffness or fixation) of the annular ligament (ring attaching the base of the stapes to the oval window), causing an air-bone gap greater than 30 dB. With a presence of BC-VEMPs, the conductive hearing loss has a low frequency or upward sloping configuration, with absence of BC-VEMPs, the hearing loss has a flat configuration, as the fixation begins to add a mass effect to the middle ear system.

Jin and colleagues (2006) assessed VEMP responses in children (2-7 years of age) before and after undergoing cochlear implantation. Six of 12 children exhibited normal VEMP responses prior to CI surgery. Of the six children with VEMPs preoperatively, five demonstrated an absence of VEMPs and one showed a decrease in VEMP amplitude following implantation. VEMPs were absent in 11 of 12 children while the implant device was turned off. Once the CI devices were turned on, four children had recordable VEMP responses, including one that had preoperative and postoperative VEMPs when the CI was turned off as well. The reduction and or abolition of VEMPs following implantation suggest a reduction in saccular function postoperatively, likely due to the saccule's susceptibility to damage during CI surgery because of its proximity to the point of electrode insertion. In three of the four children with absent VEMPs preoperatively and present VEMPs with CI stimulation, two had Mondini malformation and one had an absence of a portion of the VIIIth cranial nerve. The authors suggested that the presence of VEMP responses when the CI was turned on was induced by stimulation of the vestibular nerve in these patients. Overall, however, CI stimulation did not additionally stimulate the vestibular nerve.

Wang and colleagues (2006) assessed VEMP responses in patients following acoustic trauma, resulting in hearing loss. Abnormal VEMPs were found in 38% of the affected ears. Following treatment with medication (including isosorbide for patients with low frequency hearing loss and a combination of dextran, gingko biloba, vitamin B complex and a minor tranquilizer for all others), 44% of ears with normal VEMPs demonstrated hearing recovery. However, of ears with absent VEMPs, none experienced improvement in hearing thresholds. A significant relationship was found between the

presence of VEMPs and hearing outcome following acute acoustic trauma (sensitivity 44% and specificity 100%). This further shows that loud noise not only can be deleterious to the function of the cochlea, but may also result in saccular impairment. Therefore, patients with absent or delayed VEMPs after acoustic trauma indicate damage in the sacculocollic reflex pathway as well as damage to the cochlea resulting in irreversible hearing loss. Based on the unexpected predictive value of VEMPs, the authors suggested the use of VEMP assessment in patients who present with symptoms of acute acoustic trauma. However, it must be remembered that the presence of VEMPs in these individuals does not necessarily predict a recovery of hearing thresholds.

Due to the close proximity of the saccule to the stapes footplate, as mentioned above, intense sounds my cause damage to the saccule much like it does to the cochlea. Wang and Young (2007) evaluated VEMPs in subjects with noise-induced sensorineural hearing loss (SNHL). In these subjects, only 10 of 20 (50%) had normal VEMP responses. When used in conjunction with caloric testing, 70% of subjects with noise-induced hearing loss had some vestibular abnormality. The degree of SNHL at 4 kHz was correlated with VEMP responses, but not caloric responses. Specifically, in subjects with a hearing threshold greater than 40 dB HL at 4 kHz, presumed increased damage to the saccule resulted in abnormal VEMPs. It was hypothesized that saccular damage resulting from noise exposure may be due in part to a reduction in blood flow in the saccule, much as the cochlea is deprived from an adequate blood supply with noise-induced hearing loss. Additionally, the authors pointed out the degree of vestibular abnormality (70%) was greater than the number of subjects complaining of vertigo (45%)

and, therefore, suggested asymptomatic vestibular malfunction associated with noise-induced hearing loss.

VEMP Responses in Patients with Vestibular and Central Disorders

The VEMP pathway includes the saccular macula and its primary neurons, vestibulospinal neurons arising from the lateral vestibular nucleus, the medial vestibulospinal tract, and the ipsilateral motor neurons of the SCM muscle. A lesion lying anywhere throughout this pathway could result in abnormal or absent VEMPs (Shimizu et al., 2000). VEMP testing has proven to be useful in identification and progression of various vestibulopathies, including Ménière's disease, ototoxicity, neuritis, vestibular schwannoma, and Superior Canal Dehiscence. VEMP testing may also prove beneficial in assessment of patients with Multiple Sclerosis and/or brainstem pathology.

Ménière's Disease

Ménière's disease results in degeneration of hair cells in the cochlea and vestibular structures, including the saccule (Akkuzu et al., 2006). De Waele (2001) found absent VEMPs in 54% of subjects with Ménière's disease, however, in 46% of these subjects, VEMP latency and peak-to-peak amplitude did not differ significantly from that of normal subjects. The author further went on to predict, based upon their results, that VEMPs could be indicated to assess the likelihood of a Ménière's patient to suffer from drop attacks of saccular origin. In this study, no correlation was found between semicircular canal (SCC) paresis and the absence of VEMP responses. This further demonstrates that the VEMP does not arise from the SCCs. Other authors have

suggested that VEMP amplitude is determined by the presence and severity of saccular hydrops. That is, the more extensive the hydrops, the more likely that the VEMP amplitude will be greatly reduced or absent (Young, Huang & Cheng, 2002). Akkuzu et al. (2006) found absent VEMPs in 20% of subjects with Ménière's disease and prolonged latencies of wave p13 in 30% of subjects, for a total of 50% of Ménière's disease presenting with abnormal VEMP results (compared to 5.9 % of normals presenting with abnormal findings). Only one of these individuals had an abnormal asymmetry ratio. (This may be due in large part to the highly variable asymmetry ratios found for normal individuals.) The abnormal VEMP responses are likely due to hydrophic damage to the saccule. No significant difference was found between affected and unaffected ears in Ménière's subjects when comparing mean p13 and mean n23 latencies and peak-to-peak amplitude. Additionally, no significant correlation was observed between severity of disease and VEMP responses, although this may warrant further investigation with a larger sample size. In contrast to the findings mentioned above, Picciotti and colleagues (2005) found no significant difference in presence, latency or amplitude ratio of patients with Ménière's disease (n=11) when compared to normal individuals.

When using tone bursts of various frequencies, Node and colleagues (2005) found a higher peak amplitude frequency for patients with endolymphatic hydrops when compared to normals, although wave latencies were consistent across groups. Namely, VEMP amplitudes were greatest between 700 and 1000 Hz (mode = 1000 Hz) in patients with endolymphatic hydrops, while in normals, amplitude was greatest at 500 and 700 Hz. Additionally, patients experienced a shift in their VEMP characteristic frequency following Furosemide administration. However, peak amplitude was not correlated with

stage of disease, duration of disease, time since last episode or presence of canal paresis. What causes a chance in VEMP frequency of peak amplitude in patients with endolymphatic hydrops? The authors hypothesized that the saccule behaves much like a balloon, that when expanded (as in the case of hydrops), best produces or responds to sounds of higher frequencies. In the absence of hydrops, the saccule is much like a deflated balloon that produces a sound of a lower frequency.

A group of researchers (Lin et al., 2006) looked at VEMP responses in asymptomatic ears of Ménière's patient in comparison to VEMP responses in affected ears and in normal ears of a control group. Using varying frequencies of tone burst stimuli to evaluate VEMP thresholds and VEMP tuning, they determined that 27% of asymptomatic ears demonstrated elevated thresholds and altered tuning much like the results found in ears with confirmed Ménière's disease in the Node et al., 2005 study. In a study of human temporal bones, they also found 35% of asymptomatic ears exhibited saccular endolymphatic hydrops. Based on these findings, they made two strong conclusions: 1) symptoms of Ménière's disease are preceded by endolymphatic hydrops and 2) VEMPs seem to be sensitive to hydrophic changes in the saccule and, therefore, may be useful in identifying asymptomatic endolymphatic hydrops and the prognosis for the eventual development of bilateral Ménière's disease. Further study is under way to determine the predictive value of VEMPs in the development of bilateral Ménière's disease.

Kuo, Yang & Young (2005) assessed VEMP responses in subjects with Ménière's disease immediately following an attack of vertiginous symptoms. Twenty-four hours after the onset of the attack, 67% of the patients had abnormal VEMP responses,

suggesting that Ménière's attacks originate (at least partially) from the saccule. Forty-eight hours after the onset, however, only 33% had abnormal VEMPs. The improvement seen in some patients was likely due to drainage of the saccular hydrops. On the other hand, the subjects who had no recovery from abnormal VEMPs perhaps suffered from a more devastating rupture of the saccular membrane and its collapse onto the sensory epithelium. The saccule does not recover from such an injury and absent VEMPs will persist in these patients.

A correlation was found between severity of low frequency (250-1000 Hz) hearing loss in patients with Ménière's disease and the absence of ipsilateral VEMPs. In one study, all patients with low frequency hearing loss exceeding 60 dB had absent VEMPs. On the other hand, patients who exhibited high frequency (4-8 kHz) hearing loss of the same severity could still have intact VEMPs (de Waele, 2001). Young, Wu & Wu (2002), on the other hand, found normal VEMPs in all their patients tested with low-tone hearing loss. They attribute these confounding results to the characteristics of the patient population. In the study by de Waele (2001), older subjects were used, possibly with more extensive or severe saccular disease. Young and colleagues' (2002) subjects had a mean age of 28 years and were likely only in the beginning stages of the disease.

In some subjects with Ménière's disease and delayed endolymphatic hydrops associated with unilateral deafness, contralateral fluctuating hearing loss, and episodic vertigo, oral glycerol administration was found to improve VEMP responses that were previously absent, providing further proof that Ménière's disease in some patients may result from endolymphatic hydrops (Murofushi et al., 2001; Ohki et al., 2002; Magliulo et al., 2004[2]). Additionally, VEMP assessment following the oral administration of glycerol

has been found to be a test capable of identifying saccular dysfunctions that are otherwise undetectable with routine methods of vestibular assessment, particularly endolymphatic hydrops (Magliulo et al., 2004[1]; Magliulo et al., 2004[2]). Magliulo and colleagues (2004[1]) used glycerol to monitor improvements in both Distortion Product Otoacoustic Emissions (DPOAEs) and VEMPs. They found improvements in both in some subjects as well as improvements in one or the other in some subjects. They concluded that improvements in both DPOAEs and VEMPs suggested an endolymphatic hydrops that affected both the anterior and posterior parts of the labyrinth, whereas improvement in only one of the responses suggested hydrops in only one of the endolymphatic compartments. They found, then, that VEMPs and DPOAEs with glycerol administration may allow for the early diagnosis of endolymphatic hydrops and suggested that these tests become routine clinically in patients complaining of vestibular and audiological symptoms. Subjects whose VEMPs did not improve following glycerol administration may suffer from irreversible damage to the hair cells of the saccule. On the other hand, if VEMPs did improve following administration of glycerol, the subjects may suffer from endolymphatic hydrops in the saccule that could be reversible (Murofushi et al., 2001).

Ototoxicity

Gentamicin treatment for Ménière's disease has been found to abolish VEMP responses bilaterally one month after the initiation of treatment. This absence of VEMPs persisted six months to one year after treatment on the injected side, providing proof that gentamicin is effective at desensitizing the saccule, at least to stimulation by high clicks (de Waele, 2001; Picciotti et al., 2005). One study showed a reappearance of VEMPs in

2 of 12 patients following gentamycin injection, although caloric responses remained unchanged. These two patients were followed the longest of those involved in the study (28 months). The authors of the study suggested that this observed recovery of VEMPs indicated a regeneration of saccular cells over time that is independent of regeneration of ampullar cells. Additionally, they stated that the recovery seen with long follow-up confirms the need to follow patients long-term post- gentamycin treatment (Picciotti et al., 2005). Although, VEMP abolition occurred in all patients undergoing gentamicin injection, unilateral abolition of the horizontal SCC only occurred in approximately 50% of patients, suggesting that the saccular macula are more sensitive and susceptible to Gentamicin than is the ampulla of the horizontal SCC (de Waele, 2001; Picciotti et al., 2005).

The effect of irradiation on VEMP responses was assessed in a study by Chen and colleagues (2002). They found normal VEMPs both prior to and following irradiation treatment for nasopharyngeal carcinoma in most patients. Wu, Young & Ko (2003) found that irradiation did have an affect on VEMP responses. They found prolonged latencies of the p13 and n23 waves compared to normal ears. Specifically, they found that latency increased as did the amount of irradiation received. A correlation was also found between the occurrence of radiation otitis media and delayed VEMPs, while delayed VEMPs were unrelated to sensorineural hearing loss or canal paresis caused by the radiation. They further suggested that delayed VEMPs following irradiation could be due to radiation-induced brainstem lesions affecting the sacculocollic pathways, but also posited that it could be due to irradiated neck tissues. The differences found between the two preceding studies could be due to the very small sample size (n=6) in the Chen et al.

(2002) study compared to the larger sample size (n=22) used in the Wu et al. study (2003). Overall, we can conclude that VEMP testing may be used to predict balance problems in subjects undergoing irradiation therapy (Wu et al., 2003).

Vestibular Neuritis

Vestibular neuritis (neurolabyrinthitis) is characterized by sudden vertigo lasting hours or days in response to an acute loss of peripheral vestibular function (Murofushi et al., 1996). In approximately half of the patients with vestibular neuritis, abnormal or absent VEMPs were observed unilateral to the side of the lesion. This suggests that the saccular nerve and the inferior portion of the vestibular nerve may not always be affected in patients with vestibular neuritis (Murofushi et al., 1996; de Waele, 2001; Chen, Young & Tseng, 2002). Brantberg, Tribukait & Fransson (2003) looked at the use of skull tap induced VEMPs in patients with vestibular neuritis. In this procedure, gentle skull taps are delivered above each ear and on the midline of the forehead. Abnormal VEMPs using skull taps were found in 56% of vestibular neuritis patients, compared to 22% seen with click-evoked VEMPs. The authors suggested that there might be an additional component that is responsible for the VEMP resulting from skull tap other than the inferior portion of the vestibular nerve, because this division of the vestibular nerve is often spared in vestibular neuritis. Benign paroxysmal positional vertigo (BPPV) has been found to occur frequently following vestibular neuritis. A correlation was found between the presence of VEMPs in subjects with vestibular neuritis and development of BPPV within two years following onset of the disease. Therefore, vestibular neuritis

patients with absent VEMPs due to involvement of the inferior vestibular nerve cannot develop SCC-type BPPV (Murofushi et al., 1996; de Waele, 2001).

Vestibular Schwannoma

Both normal and abnormal VEMPs may be observed in patients with vestibular schwannoma, depending on the size and extension of the tumor onto the inferior portion of the vestibular nerve (de Waele, 2001). Halmagyi & Curthoys (1999) found abnormal VEMP (low amplitude or absence) in four out of five patients with vestibular schwannoma, while 89% of Chen, Young & Tseng's (2002) patients with vestibular schwannomas (CPA tumors) displayed absent VEMPs. Chen and colleagues (2002) further found that the average tumor size of subjects exhibiting absent VEMPs was 2.6 cm, while the average tumor size of subjects with present VEMPs was 1.2 cm. (See also Patko et al., 2003.) When present, VEMP thresholds for the lesioned side in subjects with vestibular schwannoma were found to be elevated compared to the contralateral side, resulting in abnormal asymmetry between the two ears (Ochi et al., 2001). Based on these findings, VEMPs could aid in diagnosing vestibular schwannoma when used collectively with other audiological, vestibular, and electrophysiological measures (Halmagyi & Curthoys, 1999; de Waele, 2001).

Additionally, prior to undergoing surgery for vestibular schwannoma, VEMP assessment can be used to predict the site of lesion on the vestibular nerve (inferior portion versus superior portion) so that surgical decisions can be made. Patients with absent caloric responses and VEMPs exhibit the presence of a tumor involving both the inferior and superior divisions of the vestibular nerve. On the other hand, patients who

present with normal caloric responses and absent VEMPs demonstrate a tumor of the inferior vestibular nerve alone. Following surgery, VEMP responses can be used to evaluate any residual inferior vestibular nerve function and whether the tumor was a compression tumor or an infiltrating tumor (Chen, Young & Tseng, 2002). Chen and colleagues (2002) had a patient who presented with an epidermoid cyst. This subject had absent VEMPs, absent caloric responses, and hearing loss. However, following tumor removal surgery, all three had fully recovered. This suggested that the epidermoid cyst was a compression tumor, as opposed to an infiltrating tumor (vestibular schwannoma) in which responses on these tests are irreversible.

Neurofibromatosis 2 (NF2) is a condition that is characterized by neurofibromas (fibrous tumors composed of nervous and connective tissue and produced by proliferation of Schwann cells), typically bilaterally. Symptoms of this disorder include hearing loss, facial paresis, blurred vision, and headache. Neurofibromas may arise from the superior or inferior portion of the vestibular nerve. Wang, Hsu & Young (2005) looked at caloric and VEMP responses in subjects with NF2. They found that caloric responses were much more often affected (71% of the time) than were VEMP responses (14% of the time) in these subjects, suggesting that NF2 neurofibromas arise most often from the superior vestibular nerve. The only NF2 subject that did present with absent VEMPs suffered from a large tumor. Wang and colleagues, therefore, suggested the use of VEMP testing to assess the degree of tumor infiltration in NF2 patients.

Superior Canal Dehiscence (Tullio Phenomenon)

Superior Canal Dehiscence (SCD) is a syndrome of vertigo and oscillopsia induced by loud sounds or changes in middle ear or intracranial pressure. SCD is often accompanied by an audiological air-bone gap in the low to mid frequencies and sensitivity to bone conducted sounds (Minor, 2005). SCD subjects who present with the Tullio effect (torsional nystagmus beating away from the affected ear induced by loud sounds) or Hennebert sign (nystagmus beating away from or toward the affected ear induced by positive and negative pressure in the ear canal, respectively) have abnormally large VEMP amplitude (greater than 500 μV) and abnormally low VEMP thresholds (greater than 20 dB lower than in normal subjects) (Halmagyi & Curthoys, 1999). Minor (2005) found abnormally low VEMP thresholds in patients with SCD (n = 65) as well. Specifically, he found that the VEMP threshold in affected ears (mean 81 ±9 dB nHL) were significantly different than VEMP thresholds for unaffected ears (mean 99 ±7 dB nHL) and ears of normal controls (mean 98 ±4 dB nHL). A criterion of VEMP thresholds 85 dB nHL or less was suggested as a positive indicator of SCD.

Abnormally low VEMP thresholds in these patients are thought to arise from dehiscence (opening/thinning) of the bone of the superior semicircular canal (SCC). This area of reduced bone can act as an additional area of stimulation resulting in increased transmission of sound through the vestibule to the saccule (Colebatch, 2001; Minor, 2005). Radiologic findings in patients with SCD often show this to occur bilaterally, however, it may be the case that only one side is symptomatic. Reduced VEMP thresholds are only found on the symptomatic side, suggesting that superior SCD may be congenital in nature and may not always be symptomatic (Colebatch, 2001). Minor (2005) suggested that patients who present with an unexplained air-bone gap, be tested

with VEMPs. Remember that air conducted VEMPs are absent in the presence of conductive hearing loss. However, a patient that has SCD may demonstrate an audiological air-bone gap in the presence of VEMPs, particularly at very low thresholds.

Modugno and his colleagues (2006) studied patients who had abnormally low VEMP thresholds with CT scans that showed normal features ruling out SCD. All patients had vertigo and history of trauma. In two of the patients, exploratory tympanotomy revealed perilymphatic fistula. In one patient following fistula repair, VEMP thresholds returned to normal values. In two of the other cases, where fistula could not be identified, patients demonstrated an increase in VEMP thresholds within normal limits that correlated with recovery of symptoms of vertigo. One patient did not fully recover from fistula even after initial and revision surgeries. The authors of this study suggested that lowered VEMP thresholds might arise from the perilymphatic fistula reducing inner ear impedance or possible failure of the middle ear muscles to contract to intense stimuli.

Enlarged vestibular aqueduct (LVA) is a congenital Mondini-type inner ear anomaly that often shows bilateral early onset, progressive hearing loss in children. Measurements of the inner ear components using CT scan reveal abnormally large dimensions. Obtained VEMP responses in patients with LVA showed larger amplitude and lower threshold. Like superior SCC dehiscence and the Tullio phenomenon, openings (or abnormally large openings, in the case of LVA) provide an additional mode of stimulation, causing larger displacement of the sensory organs to acoustic and pressure changes (Sheykholeslami et al., 2004).

Benign Paroxysmal Positional Vertigo (BPPV)

Benign Paroxysmal Positional Vertigo (BPPV) results from a dislodging of otoliths from the utricle and their gathering in the semicircular canals where they stimulate the cupula. The same process by which damage is done to the utricle may affect the saccular macula (Akkuzu et al., 2006). One study found normal VEMPs bilaterally in patients with BPPV and/or psychogenic vertigo (Heide et al, 1999). Another, larger study found abnormal VEMP responses in 30% of BPPV subjects (compared to 5.9% abnormality in normal subjects); the majority of these responses were abnormal due to delayed latencies of p13, a lesser number of individuals also exhibited delayed n23 latencies and only one subject demonstrated an abnormal asymmetry ratio (Akkuzu et al., 2006). The researcher went on to suggest a possible role of the utricle in the VEMP reflex arc thereby affecting VEMPs in subjects with BPPV. Further research is needed to assess a possible utricular influence on the VEMP.

Stroke

Abnormal VEMPs may also be found in patients with more central lesions of the vestibulocollic pathway (Heide et al, 1999). Abnormal VEMP responses were observed in 79% of patients recovering from brainstem stroke. The abnormal findings increased to 93% in this population once caloric irrigation was also completed. While caloric irrigation assesses the vestibulo-ocular reflex traveling up through the upper brainstem, VEMP measurement assesses the sacculocollic reflex traveling down through the lower brainstem. Therefore, the two tests can be used together to better evaluate the extension of brainstem stroke. For example, if a patient has abnormal VEMPs in the presence of

normal caloric response, interruption of the descending pathway from the brainstem is affected (Chen & Young, 2003; see also Karino et al., 2005). One study showed a significant decrease in VEMP thresholds on the side with Wallenberg (lateral medullary) syndrome, with no difference in VEMP latencies noted between the affected and unaffected sides. VEMP thresholds returned to normal values as patient's symptoms of nystagmus, diplopia, ataxia and Horner's syndrome improved. The authors argued that brainstem (medullary) stroke mainly affects VEMP amplitude responses, rather than VEMP latency (Deftereos et al., 2006; see also Pollak et al., 2006). Absent VEMPs were also found to correlate with hemorrhage at the level of the pons found on MRI scanning (Chen & Young, 2003; see also Pollak et al., 2006). Pollak and colleagues (2006) found no correlation between VEMP responses and cerebellar stroke.

Multiple Sclerosis

VEMP latency was found to be delayed in subjects with Multiple sclerosis (MS). This is likely due to decrease in myelination of the afferent axons of the vestibulospinal tract (Shimizu et al., 2000; Sartucci & Logi, 2002; Version et al., 2002; Alpini et al., 2004). VEMPs may also be absent in MS patients depending on the severity of neural transmission dysfunction (Alpini et al., 2004). In one study, VEMPs were abnormal in 31% of patients with MS, while 38% had abnormal ABR responses and 21% had abnormal tilts of the Subjective Visual Vertical (SVV). MRI detected brainstem lesions in 37.5% of patients and cerebellar demyelinating lesions in 41.7% of patients with MS (Versino et al., 2002). Alpini and colleagues (2004) found abnormal VEMPs in over 50% of MS patients. VEMP amplitude was also decreased in some MS patients.

Sartucci & Logi (2002) suggested that reduced amplitudes are due to either a dysyncronization of firing of the vestibulospinal fibers resulting in less spatial summation of the motor neurons or a partial block in conduction resulting in a reduced discharge at the motor neuron level. VEMPs were found to correlate with clinical findings of the presence or absence of brainstem involvement in 55% of MS patients, while MRI was found to correlate in 65% of the MS patients. Additionally, VEMPs were abnormal in 10% of MS patients exhibiting normal MRI and no specific clinical signs, indicating brainstem dysfunction (Alpini et al., 2004). VEMPs should be included in the test protocol for patients in the assessment of brainstem dysfunction. However, one author suggested that ABR should be considered the preferred method of assessment of brainstem function in MS patients complaining of dizziness (Versino et al., 2002). On the other hand, Sartucci & Logi (2002) found an overall sensitivity of 60% for VEMPs, which is better than that for ABR in MS patients.

Other Disorders That May Affect VEMPs

VEMP testing may also provide prognostic information regarding vertigo following head trauma. These patients may have normal caloric and rotation test responses, normal SVV, and normal off-vertical axis rotation (OVAR) if the horizontal SCC is spared or if vestibular compensation has already occurred. In these patients, VEMPs may be the only test indicating the presence of otolithic lesion secondary to head trauma. Absence of VEMPs is persistent and can, therefore, clue a clinician into the presence of a chronic, compensated lesion (de Waele, 2001). Since the sacculocollic reflex pathway passes through the area of the basilar artery, Liao & Young (2004)

decided to look at VEMP responses in patients with basilar artery migraine. Some of these patients exhibited absent or delayed VEMPs, possibly due to interruption in the sacculocollic pathway due to hyperfusion in the area of the basilar artery.

Ozeki and colleagues (2006) used click- and galvanic-evoked VEMP recordings in conjunction with caloric testing to assess the site of lesion in Herpes Zoster Oticus. Also known as Ramsay Hunt syndrome (RMH), Herpes Zoster Oticus is a condition thought to be caused by the reactivation of latent varicella-zoster virus. Typical symptoms of RMH include auricular vesicles (blisters/cysts around the ear), facial paralysis and vestibulocohlear dysfunction (including SNHL, tinnitus and/or vertigo). The researchers found 70% of patients (total n = 10) had abnormal (absent or delayed) VEMPs. VEMPs in response to galvanic stimulation were absent in 50% of those tested (total n = 4). Caloric testing showed abnormal responses in all affected ears. Neither VEMP nor caloric responses were found to correlate with the degree of hearing impairment observed. It was concluded that canal paresis is the most common finding with RMH, with most patients also having involvement of the inferior vestibular nerve and/or saccule. When VEMPs are present to galvanic stimulation only, the authors suggested that the site of lesion is likely to be primarily in the labyrinth. Whereas, absence to both click- and galvanic-evoked stimuli suggests lesion of the vestibular nerve (and possibly the labyrinth as well).

Another interesting use of VEMP testing was explored by Tal et al. (2006). They found a significant difference between VEMP thresholds for individuals who were susceptible to seasickness and individuals who were not. Specifically, individuals who are susceptible to seasickness had a higher VEMP threshold and lower peak-to-peak

amplitude than individuals who were not susceptible to seasickness. The authors suggested a possible reduction in otolith function, which could result in increased discrepancy between information from the various sensory systems involved in the sensation of motion, resulting in higher susceptibility to seasickness.

Abnormal VEMPs with Normal Caloric Responses

As seen with some of the disorders mentioned above, absent VEMPs are sometimes observed in the presence of normal caloric responses and overall normal ENG results (in about 5% of patients). Some specific instances may include cases of Ménière's disease in which the endolymphatic hydrops specifically targets the saccule, Vestibular schwannoma that primarily affects the inferior portion of CN VIII, and multiple sclerosis. Some authors have coined the term Inferior Vestibular neuritis to refer specifically, to viral infection of the inferior vestibular nerve that clinically presents with absent VEMP responses (Iwasaki et al., 2005). Clinical presentation of specific pathology of the saccule and/or posterior semicircular canal would likely result in a vertical or vertical-torsional nystagmus. Patients may subjectively report torsional or vertical vertigo (Iwasaki et al., 2005).

TABLE 1. Disorders that may affect VEMP responses. (Not exhaustive.)

Disorders	Symptoms	VEMP Results	VNG/Audio Results	Other Important Considerations
Ménière's Disease	Vertigo lasting hours at a time, aural fullness, roaring tinnitus, low frequency (possibly fluctuating) SNHL, nausea and vomiting	May be absent, normal, or occur at delayed latencies (P13). Abnormal VEMPs may be correlated with stage of episode/disease.	Audio may show low frequency SNHL, VNG may be normal depending on stage of disease/episode	Some authors suggest that VEMP amplitude is determined by the extent of saccular hydrops. Other authors found peak amplitude at a higher frequency (when using tone burst stimuli) with presence of hydrops.
Ototoxicity (Gentamicin)	Temporary or permanent disturbances in hearing	Absent, may return after a couple of years		

	and/or balance. Varying in affects systems and severity of dysfunction.	in some patients.		
Irradiation	Similar to ototoxicity, depending on site of radiation and extent of radiation.	Normal; may demonstrate delayed latencies		Delayed VEMPs may result from radiation-induced brainstem lesions or due to irradiated neck tissue. May be used to predict balance problems following radiation therapy.
Vestibular Neuritis	Sudden vertigo lasting hours or days in response to an acute loss of peripheral vestiblar function. May be accompanies with nausea and vomiting, fever, abnormal gait, balance problems, "pins and needles" sensations.	Abnormal on side of lesion in ~50%	Abnormal, with unilateral caloric loss. May have spontaneous nystagmus, headshake nystagmus and nystagmus following head thrust.	Authors suggest presence of VEMPs may be determined by involvement of the saccular nerve and/or inferior vestibular nerve. VEMP presence is correlated with occurrence of BPPV within two years.
Vestibular Schwannoma	Tinnitus and SNHL in the affected ear, vertigo; may include headache, word disproportionately poor word recognition ability, loss of balance, numbness/pain in face or one ear and/or vision abnormalities.	May be normal or abnormal (absent or increased threshold resulting in interaural asymmetry) depending on size and extension of tumor onto IVN.	If absent caloric responses as well, tumor may involve both the inferior and superior portions of the nerve. If calorics normal, likely only inferior portion of nerve affected.	May be used to assess residual vestibular function following tumor revmoval.
Neruofibromatosis 2 (NF2)	Neurofibromas typically bilaterally, SNHL, facial paresis, blurred vision and headache.	Normal, rarely affected.	Calorics most often affected suggesting superior nevre involvement.	
Superior Canal Dehiscence (SCD)	Vertigo and oscillopsia induced by loud sounds or changes in middle ear or intracranial pressure.	Abnormally large VEMP amplitude and abnormally low VEMP threshold (85 dB nHL or less).	Audiological air-bone gap in the low and mid frequencies due to sensitivity of bone conducted sounds.	Results similar for perilymphatic fistula
Enlarged vestibular aqueduct (LVA)	Bilateral, early onset sudden, fluctuating and/or progressive SNHL, particularly in children. Abnormally large dimension on CT scan of the inner ear components.	Same as SCD		
BPPV	Vertigo evoked by rapid head/body movements	Normal, some authors suggest delayed latencies in some patients	Positive Hallpike for BPPV, audio unaffected.	
Brainstem Stroke	Weakness/paralysis, numbness/tingling, nystagmus, vision changes, ataxia, etc. Varies depending on location and extent of stroke.	Abnormal (absent or reduced amplitudes)	Calorics may also be abnormal; central pattern	For stroke at the level of the medulla and pons. No correltation between VEMP responses and cerebellar stroke.
Multiple Sclerosis	Weakness/paralysis/tremor of one or more extremities, muscle spasicity, muscle atrophy, decreased coordination, vertigo, SNHL, etc. Varies dependent on the degree of demyelination.	Delayed latencies, may be absent depending on the severity of neural transmission dysfunction		

Conclusions

Measurement of VEMP is reliable (depending on the test conditions), tolerable (does not induce nausea) and is noninvasive (Halmagyi & Curthoys, 1999; de Waele, 2001). VEMP testing is simple and can be completed quickly (in as little as 3 minutes) using the same equipment that is used for measuring auditory brainstem responses (Halmagyi & Curthoys, 1999). VEMP responses are large with high reproducibility and can be analyzed quickly using computer software (Brantberg & Fransson, 2001). Colebatch & Halmagyi (1992) recommended VEMP assessment as a simple procedure that is clinically applicable and that could provide novel information about vestibular function that is not already explored via caloric or rotation testing or tests of utricular function (Halmagyi & Curthoys, 1999; see also Karino et al., 2005). Typical vestibular tests effectively assess the function of the superior vestibular nerve. Uniquely, VEMPs assess the function of the inferior vestibular nerve. Therefore, adding VEMPs to a standard vestibular protocol can allow clinicians to separately evaluate the function of both branches of the vestibular nerve (Iwasaki et al., 2005). The main advantage of VEMP testing is that it allows us to assess each saccule individually and objectively (Tran Ba Huy & Toupet, 2001). Not only are VEMPs effective at assessing the function of the saccule and afferent nerve fibers, they are also able to evaluate the vestibulospinal (sacculospinal) pathways (de Waele, 2001). Currently, the only two clinical tests that evaluate the vestibulospinal pathways are VEMPs and posturography. While posturography is not clinically feasible for all patients, particularly those with difficulty standing, VEMPs can be assessed in subjects so long as they are able to sit upright (Alpini et al., 2004). Heide and colleagues (1999) found a sensitivity and specificity of

59% and 100% respectively for VEMPs (in patients with acute vertigo presumed to be vestibular in nature). Bone conduction is alternative mode of VEMP collection that is a quick, convenient, and non-invasive test of vestibular function in patients with conductive hearing loss (Sheykholeslami et al., 2001[1]).

Assessment of VEMPs is relatively simple to perform, and has diagnostic, prognostic, and therapeutic value. VEMPs are not affected by sensorineural hearing loss. However, they show some characteristic differences between individuals with normal vestibular function and those with pathology that targets the sacculocollic pathway. This review has shown how Ménière's disease may affect the VEMP response, not only by increasing VEMP threshold, but also by changing the frequency selectivity of the saccule for the VEMP response. Additionally, testing the VEMP response could provide an indication of possible problems with postural control for Ménière's patients, particularly if they are older and/or have a strong visual dependence. VEMP testing could help identify these patients so that appropriate vestibular rehabilitation, with a focus on postural stability, could be initiated. More histopathological studies need to be conducted in order to determine the mode by which VEMPs become abnormal in patients with Ménière's disease (Young et al., 2002). Monitoring via VEMP assessment may be a useful tool to incorporate for individuals who are taking known ototoxic medications. VEMP testing can be used to detect effects of Gentamicin injection and the possible presence of a vestibular schwannoma (de Waele, 2001). Some authors have suggested that VEMP assessment may be the most useful test in detection of vestibular schwannomas, because they most often arise from the inferior portion of the vestibular

nerve. Therefore, VEMPs may be especially helpful in identifying the particular portions/nerves that are involved (Ochi et al., 2001).

By measuring VEMP thresholds, even in the presence of an air-bone gap, SCD may be identified (Minor, 2005). Also, VEMP assessment can be used to help determine whether or not patients with vestibular neuritis will develop BPPV (de Waele, 2001). VEMP measurement is a useful clinical tool for assessment of the function of the vestibulospinal tract and may be helpful in detection of subclinical lesions of the vestibulospinal tract that are associated with MS (Shimizu et al., 2000). VEMPs may eventually hold some promise in the evaluation of brainstem lesions, especially when used in conjunction with ABR and other neurophysiological tests (Heide et al., 1999; Versino et al., 2002; Deftereos et al., 2006). More research needs to be done to assess the possible utility of VEMP testing in patients with brainstem stroke, especially in conjunction with MRI scans to determine anatomical correlations to VEMPs (Pollak et al., 2006). VEMP testing may also be used intraoperatively to monitor or guide surgical procedures, either directly via electrical stimulation of the inferior vestibular nerve or indirectly via clinical means (Basta et al., 2005[2]). VEMP evaluation may have some utility in guiding vestibular rehabilitation by determining the vastness of disease and the presence of residual vestibular function (de Waele, 2001).

Specific limitations associated with VEMP testing are 1) the requirement of patient cooperation, 2) difficulty in testing patients with neck stiffness or inability to maintain tonic muscle activity in the SCM muscle, and 3) absent responses with conductive hearing losses (Halmagyi & Curthoys, 1999; Colebatch, 2001; Deftereos et al., 2006). In lieu of these limitations, VEMPs provide a simple means of obtaining

information about the function of the vestibulo-collic pathway, the saccule, and its nerve fibers. Although it cannot alone provide disease specific information, it should be used clinically as a complement to the existing test battery to detect saccular, inferior vestibular nerve, and/or brainstem dysfunction (Alpini et al., 2004). Colebatch (2001) suggested that a patient should not be diagnosed as having a total vestibular loss without completion of VEMP assessment.

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